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WO 092017768 A

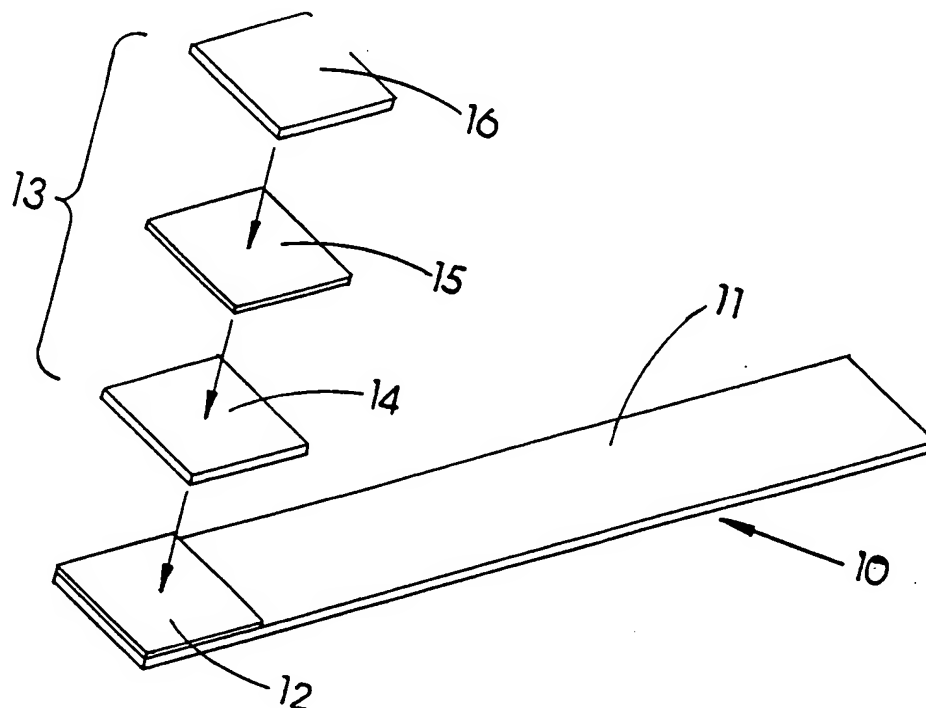
OCT 1992

INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

✓

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁵ : G01N 21/77, 31/22	A1	(11) International Publication Number: WO 92/17768 (43) International Publication Date: 15 October 1992 (15.10.92)
(21) International Application Number: PCT/US92/02611 (22) International Filing Date: 2 April 1992 (02.04.92) (30) Priority data: 681,609 8 April 1991 (08.04.91) US (71) Applicant: ENVIRONMENTAL TEST SYSTEMS, INC. [US/US]; 23575 County Road 106, Elkhart, IN 46514 (US). (72) Inventors: BLAKE, Kenneth, Allen ; 53581 Woodard Court, Elkhart, IN 46514 (US). CHRISTNER, James, Edward ; 1726 Woodland Court, Elkhart, IN 46514 (US). LUCCHESI, Leonard, John, II ; 3221 Calumet Avenue, Elkhart, IN 46514 (US).		(81) Designated States: AT (European patent), BE (European patent), CA, CH (European patent), DE (European patent), DK (European patent), ES (European patent), FR (European patent), GB (European patent), GR (European patent), IT (European patent), JP, LU (European patent), MC (European patent), NL (European patent), SE (European patent). Published <i>With international search report.</i> <div style="text-align: center; font-size: 2em;">422/56</div>

(54) Title: MULTILAYER TEST DEVICE MATRIX STRUCTURE**(57) Abstract**

A unitized multilayer dry reagent analytical chemistry test structure and device and method of fabricating such device is described. The device (10) includes two or more contiguous layers of absorbent or porous paper or polymeric material (14 and 16), at least one of which is incorporated with a test reagent composition, the layers attached to each other with an intermediate porous attachment layer (15). When the device is contacted with the fluid being tested, the attachment layer allows the free flow of

MULTILAYER TEST DEVICE MATRIX STRUCTURE

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FIELD OF THE INVENTION

The present invention relates to unitized multilayer dry reagent test device structures and to the methods and materials associated with the fabrication thereof.

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BACKGROUND OF THE INVENTION

The science of analytical chemistry and particularly simple to use dry reagent test devices using analytical chemistry principles has made dramatic progress over the past several decades. At one time such devices simply comprised a piece of filter paper impregnated with the dried residue of a pH indicator or a relatively simple test reagent composition. Devices such as these usually gave an indication of the presence or absence of a substance or a gross condition of the fluid being analyzed, such as, for example, the use of litmus paper to determine if the fluid is acidic or basic. Now such devices are much more complex in structure and composition and can give answers which are as precise, specific and sensitive as those obtained using laboratory procedures and conditions. Moreover, such devices can quite often be used without accompanying instrumentation which permit their use in the field or "on-site" to give nearly instant answers. This obviously eliminates the need for preserving sample integrity, simplifies record keeping and allows the user to take rapid corrective measures.

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Dry reagent test devices commonly consist of a bibulous or porous paper or polymeric matrix incorporating a reagent composition which reacts with the

matrix of the SERIM device is more often than not a combination or mixture of chemicals, biochemicals or immunochemicals. The more sophisticated and complicated the reagent system, the more difficult it is to
5 incorporate into the absorbent pad. For ease of formulating and manufacturing, the ideal dry reagent test device comprises a relatively simple chemical mixture incorporated into a single absorbent pad or matrix. When reagent incompatibility is encountered, it is common
10 practice to attempt separation of the various components either chemically or physically. One means commonly utilized is to separate the various components in a single matrix using selective solvent impregnation techniques. Another means is to encapsulate one reagent
15 so that it will not react with the others present in the system until it comes in contact with the fluid being tested.

More recently, it has become the practice of reagent
20 strip or SERIM device formulating scientists to separate the reagents using multilayer reagent strip devices in which the various components are retained in separate layers of the matrix until the test device is utilized. Such multilayer devices have several advantages. In
25 addition to accomplishing the separation of reagents for stability purposes, such matrices can be utilized to pretreat or concentrate the analyte or fluid being tested or to remove or complex an undesirable component or constituent in the sample fluid. It is common practice
30 in the reagent strip art to utilize multilayer matrices; however, such matrices must meet the rather strict requirement that the layers be uniformly bound to each other and that fluid must flow evenly and freely throughout the device. In this regard, to date, most
35 commercial multilayer test devices utilize a series of gel layers such as in film type devices wherein the layers are constructed by pouring one layer on top of the

soluble adhesive such as cellulose acetate. Finally, United States Patent No. 4,446,232 discloses a multilayer device in which the several layers are held together by using latex cement at the perimeter of the sandwich.

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In all of the above means of attaching layers, the problem almost invariably arises concerning the degree to which the method is effective in intimately joining the layers or if it is effective, the degree to which the flow of fluid between the layers is impaired.

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SUMMARY OF THE INVENTION

In the present invention, a method of attaching or joining layers of matrix is disclosed which is simple and extremely effective. This method of fabrication and the resulting matrix structure basically utilize a multilayer test device consisting of two or more layers of porous paper or polymeric materials or a combination thereof which are attached to one another in a contiguous face to face or end to end relationship using an intermediate attachment layer which forms an interface area between each of the matrices and permits the free flow of fluids from one matrix layer to the next. The resulting device may in its simplest configuration comprise an absorbent layer joined by means of an attachment layer. Each reagent impregnated layer is usually separately incorporated with reagent and dried prior to assembly. The intermediate attachment layer consists of a preformed fibrous material which is amenable to lamination with the paper or polymeric sheet materials and yet retains its basic porous properties.

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BRIEF DESCRIPTION OF THE DRAWINGS

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Figure 1 is a exploded perspective view of a simple reagent strip device showing the basic configuration of

which is impregnated or incorporated with a reagent, in a face to face relationship such that when the structure is contacted with the sample, the fluid may enter and flow freely between such matrices.

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The attachment layer and the utilization thereof in the fabrication of test devices is the main point of novelty of the present invention. Basically, this attachment layer material comprises an inert fibrous
10 woven or nonwoven sheet material of substantial porosity which is amenable to attachment to paper or polymeric materials such that the paper or polymeric materials become intimately bound to each other and yet does not form a barrier to the free flow of fluids or chemical
15 substances. Preferably, the attachment layer is a resilient fusible thermoplastic sheet material having "pores" of about from 0.05 mm to 1.0 mm. A "pore" is defined as the average distance between filaments. Since the attachment layers of the present invention can be and
20 preferably are non-woven fabric-like materials, the pores are usually irregular in appearance and are based on random filament placement. Exemplary of the materials that can be used in the present structure are the VILEDON nonwoven thermoplastic materials made of nylon or
25 polyester materials. Such products have a thickness of about from 0.2 to 0.6 mm, a filament diameter of about from 0.04 to 0.06 mm, and weight about from 20 to 80 grams per square meter. Obviously, depending on the application, other plastic and adhesive-like materials
30 may be used so long as the porosity and the lamination characteristics are acceptable. Other thermoplastic materials such as polycarbonates, polyethylenes, polyolefins and PVCs can likewise be used.

35 Usual materials and preparation techniques are employed to prepare the test reagents and the matrices therefor prior to and after lamination of the multilayer

system 13 consisting of a first absorbent matrix 14 and a second absorbent matrix 16 attached to each other in a face to face relationship using a nonwoven thermoplastic attachment layer 15. Either or both of the matrices 14 and 16 may be impregnated with the dried residue of a test reagent composition specific for the analyte under consideration. In this embodiment, the matrices 14 and 16 are individually impregnated with the reagent composition and then attached to each other using the attachment layer 15 and then affixed to the handle 11 using the adhesive tape 12.

Figure 2 shows a front view of a SERIM type test device 20 wherein a multilayer strip of reagent impregnated paper matrix 23 is laminated between two sheets of transparent plastic 22 (the back sheet not shown), the face portion of the front sheet being printed with marking lines 26 and a numerical scale 27 for ease of reading the extent of reaction in the matrix 23. The upper end of the matrix 23 is covered with a signal string 24 which is likewise laminated between the plastic sheets 22 but exposed to the atmosphere at opening 28. The lower end of the matrix 23 is likewise exposed to the atmosphere at opening 25 such that when the device 20 is immersed in the fluid being tested, such fluid enters the opening and wicks up the matrix by capillary action.

Figure 3 is an enlarged partial sectional view of the SERIM type test device 30 wherein the multilayer strip matrix 36 extends the entire length of the device and fluid travelling in the device essentially flows simultaneously through both of the matrices 33 and 34 held between layers of plastic 31 and 32. The multilayer strip is constructed by attaching the preprepared matrices 33 and 34 together by means of attachment layer 35 (interface area) and subsequently laminating the multilayer devices between the sheet of plastic 31 and

A second sheet of filter paper was dipped into this solution and dried at 100° C. for 10 minutes.

The first and second sheets of reagent impregnated paper as prepared above were cut into strips and attached one to the other in a face to face relationship by using an attachment layer consisting of Freudenberg VILEDON fusible web material which is a porous nylon nonwoven filament web material weighing 20 grams per square meter and having a thickness of .008 in. The lamination took place at 150°C. and utilized pressure rolls to create intimate contact of the matrices to the attachment layer and to each other. The resultant multilayer matrix structure was cut into 1/5 in. squares and attached to clear plastic handles using double faced adhesive tape.

The resultant reagent strips were stable and reacted to give varying shades of purple depending on the concentration of ketone in urine.

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Example 2 - Test for Formaldehyde in Water

Background: Formaldehyde is used extensively as a chemical sterilant; however, this compound is considered a carcinogen and must be carefully monitored. The following test can be used to detect low levels of this toxic chemical.

A device similar in structure to the one described above in Example 1 was prepared, except that the top matrix was preprepared by impregnating a piece of filter paper with a 0.1% solution of oxalyldihydrazide and 0.067 M sodium phosphate, pH 6.8 and the bottom matrix prepared with 1 mM copper sulfate. When assembled as described above in Example 1 and dipped into a solution of 10 ppm formaldehyde, the test device turned a light

INTERNATIONAL SEARCH REPORT

International Application No. PCT/US92/02611

I. CLASSIFICATION OF SUBJECT MATTER (if several classification symbols apply, indicate all)³		
According to International Patent Classification (IPC) or to both National Classification and IPC		
IPC (5): GO1N 21/77, 31/22 US CL : 422/55, 56; 436/169, 170; 435/970		
II. FIELDS SEARCHED		
Minimum Documentation Searched ⁴		
Classification System	Classification Symbols	
U.S.	422/55, 56; 436/169, 170, 810; 435/805, 970	
Documentation Searched other than Minimum Documentation to the extent that such Documents are included in the Fields Searched ⁵		
APS		
III. DOCUMENTS CONSIDERED TO BE RELEVANT¹⁴		
Category [*]	Citation of Document, ¹⁶ with indication, where appropriate, of the relevant passages ¹⁷	Relevant to Claim No. ¹⁸
X/Y	US, A, 4,776,904 (Charlton et al.) 11 October 1988, see columns 4, 7, 8 and 9.	1-3, 5, 7, 10, 12-13, 15, 17-19/ 6, 14, 20.
Y	US, A, 4,806,312 (Greenquist) 21 February 1989, see figures 4 and 5.	4.
Y,P	US, A, 5,049,358 (Lau) 17 September 1991, see abstract.	8, 9, 16.
Y	US, A, 4,061,468 (Lange et al.) 06 December 1977, see columns 2 and 3.	11.
A,P	US, A, 5,096,836 (Macho et al.) 17 March 1992, see entire document.	1-20.
<div style="display: flex; justify-content: space-between;"> <div style="width: 45%;"> <p>[*] Special categories of cited documents:¹⁵</p> <p>"A" document defining the general state of the art which is not considered to be of particular relevance</p> <p>"E" earlier document but published on or after the international filing date</p> <p>"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)</p> <p>"O" document referring to an oral disclosure, use, exhibition or other means</p> <p>"P" document published prior to the international filing date but later than the priority date claimed</p> </div> <div style="width: 45%;"> <p>"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention</p> <p>"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step</p> <p>"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art</p> <p>-- "&" document member of the same patent family</p> </div> </div>		
IV. CERTIFICATION		
Date of the Actual Completion of the International Search ²	Date of Mailing of this International Search Report ²	
15 JUNE 1992	30 JUN 1992	
International Searching Authority ¹	Signature of Authorized Officer ²⁰	
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